

2019nCoV (SARS-CoV-2) Papain-Like Proteinase (PLpro)

About Coronavirus Papain-Like Proteinase (PLpro)

COVID-19 pandemic is caused by 2019nCoV (SARS-CoV-2) infection. 2019nCoV contains 16 Non-structure protein (Nsp1-Nsp16) that may be drugable targets for antiviral compounds discovery against COVID-19¹.

2019nCoV (SARS-CoV-2) Papain-Like Proteinase (PLpro) is included in Nsp3. The coronavirus Papain-Like Proteinase (PLpro) has been found as a nucleic acid-binding domain (NAB) with a nucleic acid chaperon function, which is conserved in coronavirus, and one uncharacterized domain termed the marker domain (G2M). Following the G2M are two predicted double-pass transmembrane domains (TM1–2 and TM3–4), a putative metal binding region (ZN) and the Y domain of unknown function (subdomains Y1–3) ^{1,2}.

About Nsp3

Nsp3: Nsp3 (200 kDa) is the largest protein encoded by the coronavirus genome (SARS-CoV-2, SARS-CoV, MERS, etc.). Nsp3 is an essential component of the replication and transcription complex. It comprises various domains, the organization of which differs between coronavirus genera, due to duplication or absence of some domains. However, the N-terminal region of the Nsp3 is highly conserved among coronavirus, containing a ubiquitin-like (Ubl) globular fold followed by a flexible, extended acidic-domain (AC domain) rich in glutamic acid (38%). Next to the AC domain is a catalytically active ADP-ribose-1"-phosphatase (ADRP, *app-1"-pase*) domain (also called macro domain or X domain) thought to play a role during synthesis of viral subgenomic RNAs. SARS Unique Domain (SUD), a domain not yet identified in other coronaviruses from alphacoronavirus and betacoronavirus, follows next. The SUD domain binds oligonucleotides known to form G-quadruplexes. Downstream of the SUD domain is a second Ubl domain and the catalytically active PLpro domain that proteolytically processes the Nsp1/2, Nsp2/3 and Nsp3/4 cleavage sites^{1,2}.

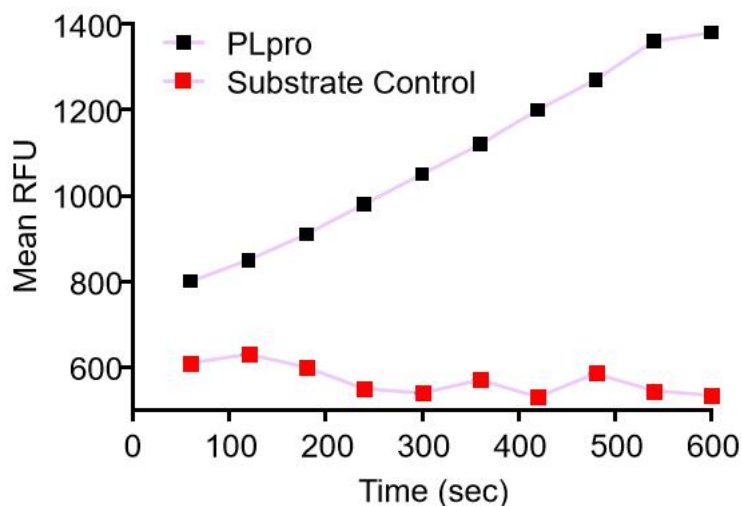
High-throughput screening (HTS) assay development of Coronavirus PLpro for antiviral compounds

HTS Approach: Fluorescence resonance energy transfer (FRET) assay for time-dependent kinetic analysis

FRET Substrate: (E-EDANS)RELNGGAPI(K-DABCYL)S (Synthetic)

Simple 2019nCoV (SARS-CoV-2) Papain-Like Proteinase (PLpro) activity assay development Protocol²:

[2019nCoV \(SARS-CoV-2\) Papain-Like Proteinase\(PLpro\) activity assay development Protocol article](#) 



References

- 1 Gordon, D. E. *et al.* A SARS-CoV-2-Human Protein-Protein Interaction Map Reveals Drug Targets and Potential Drug-Repurposing. *BioRxiv*, doi:10.1101/2020.03.22.002386 (2020).
- 2 Wojdyla, J. A. *et al.* Papain-like protease 1 from transmissible gastroenteritis virus: crystal structure and enzymatic activity toward viral and cellular substrates. *J Virol* **84**, 10063-10073, doi:10.1128/JVI.00898-10 (2010).

SARS-CoV-2 (2019nCoV) Non-structure protein (Nsp) Recombinant Antigens

- Recombinant Proteins Of SARS-CoV-2 (2019nCoV) Drugable Target For High-throughput screening (HTS) assay development of antiviral compounds against COVID-19

Name of Non-structure protein of SARS-CoV-2 (2019-nCoV, novel coronavirus)	Name of Gene in Coronavirus	GeneMedi's Recombinant Antigens For Activity Assay	High-throughput screening (HTS) assay development information and protocols
(PLpro) papain-like proteinase	Nsp3	GMP-V-2019nCoV-PLpro001	Download 
Mpro (main protease,3CLpro)	Nsp5	GMP-V-2019nCoV-Mpro001	Download 
Nsp10-CysHis,GFL protein	Nsp10	GMP-V-2019nCoV-Nsp10-01	Download 
RNA-dependent RNA polymerase(RdRP)	Nsp12	GMP-V-2019nCoV-RdRP001	Download 
2'-O-ribose methyltransferase	Nsp16	GMP-V-2019nCoV-Nsp16-01	Download 
Nsp3-X domain(Macro domain)	Nsp3	GMP-V-2019nCoV-Nsp3X-01	